had grandsons with the fragile X syndrome. As might be expected for an X-linked trait, these "transmitting males" pass the abnormality through their daughters and not their sons. Transmitting males have been said to have a "premutation" that is activated to a full mutation after passing through a female intermediate. Molecular studies now show that these transmitting males have a partial expansion of the CGG copy number in *FMR1* to the range of 60 to 200. They will donate this partially expanded CGG region as part of the X chromosome that they contribute to all of their daughters, but typically, the copy number remains unchanged. These partial expansions are, however, further amplified in a high percentage of these women during oogenesis, giving rise to the full mutation number of CGG repeats in the grandsons who then have the complete syndrome. Thus, the results of molecular analyses in families with the fragile X syndrome have explained aspects of the inheritance of the syndrome that were not previously understood.

In addition to clarifying the basis of transmitting males, molecular studies of the *FMR1* gene are elucidating the basis for the phenotypic variation in the fragile X syndrome. As many as a third of female carriers of the full-blown fragile X-CGG expansion will have some clinical symptoms, including mild mental retardation and premature ovarian failure. The reasons for this appear to be related to the phenomenon of X chromosome inactivation. True carrier females will have a copy of FMR1 that contains the expansion, is overmethylated, and cannot be expressed. The copy of *FMR1* on their other X chromosome will be structurally normal, but about half of their cells will be rendered quiescent through the process of X chromosome inactivation. Thus, such females have two populations of cells, one with normal amounts of *FMR1* and the other in which *FMR1* protein will be absent. Depending on whether the fraction of deficient cells is exactly half or not, and depending on the ratios of deficient and sufficient cells in various tissues (for example, the central nervous system), the carrier female may or may not have clinical symptoms. In males who are the offspring of women with premutation lengths of CGG repeats, mosaicism may occur so that some of their cells have undergone further expansion of the CGGs in *FMR1*. In other cells, the CGG copy number remains at the premutation level. The premutation *FMR1* genes are not methylated and presumably are expressed, but the full mutation-length CGG expansion genes are methylated and shut off. Thus, these males also have cellular mosaicism, which can have variable clinical consequences.

In addition to providing a much better understanding of the pathogenesis of the fragile X syndrome, the recent molecular advances have enhanced the study of the epidemiology of this disorder and its clinical diagnosis. The older cytogenetic tests, although still useful, are subject to several vagaries. The visualization of fragile sites is highly dependent on tissue culture and laboratory conditions as well as the skill and experience of the technician. The molecular tests are less ambiguous, so it has been possible to understand better the actual incidence of the fragile X syndrome and its full phenotypic spectrum. The availability of good diagnostic tests has already helped in the diagnosis of new patients and in giving genetic counseling to family members at risk for transmitting the disease. Prenatal diagnosis using fetal DNA derived from amniocytes, chorionic villous biopsy, or embryo biopsy is feasible and offers options for families in which this syndrome occurs. In the future, large-scale screening of newborns can be considered, but only after it is clear that early recognition of the disease would lead to some beneficial intervention to the child or the family. Ultimately, a more thorough understanding of the role of *FMR1* protein may lead to strategies for therapeutic intervention, although this may need to occur early in development. In the meantime, the summary of clinical findings and management strategies provided in the article by Hagerman should be read by all pediatricians and other clinicians who are likely to encounter patients with this common clinical problem because it provides much useful information.

LARRY J. SHAPIRO, MD
W.H. and Marie Wattis Distinguished Professor
Chair, Department of Pediatrics
University of California, San Francisco,
School of Medicine
San Francisco, CA 94143

REFERENCES

1. Hagerman RJ. Fragile X syndrome—Molecular and clinical insights and treatment issues. West J Med 1997; 166:129–137

2. Verkerk AJ, Pieretti M, Sutcliffe JS, et al. Identification of a gene (FMR-1) containing a CGG repeat coincident with a breakpoint cluster region exhibiting length variation in fragile X syndrome. Cell 1991; 65:905–914

Improving Quality Improvement: A Data-Driven Assessment

THE INEXORABLE search for quality in health care is embedded in the Hippocratic oath. Modern approaches to quality analysis in health care, however, owe as much to business reengineering strategies as they do to the scientific method. Although the literature contains many examples of successful quality interventions, it is also littered with failures. The promise of substantial improvements in quality through integrated systems and national practice guidelines has yet to be fully realized. Despite these limitations, many organizations have realized important improvements in care resulting from quality improvement activities, and a wide array of external organizations, from health care purchasers to accrediting agencies, are asking for quality information. Given this national backdrop, what are the implications of the research by Goldman and colleagues, reported elsewhere in this issue,[1] for evaluating previous quality initiatives and for identifying possibly successful strategies for future quality-related activities?

The history of modern quality improvement begins with physicians.[2] At the turn of the century, Ernest Codman, MD, evaluated the care of patients at Massachusetts

General Hospital in Boston, where he observed problems with conditions within the hospital and with documentation of the results of care delivered. In 1917 the American College of Surgeons established a hospital standardization program that used a series of minimum standards to evaluate care. In the 1950s, the Joint Commission on the Accreditation of Hospitals was created by various national organizations to assess the quality of care. At first it used these minimum standards, but in the 1960s and 1970s, the focus shifted to optimal achievable results and standardized audits of medical staff functions such as surgical case review (quality assurance). Now the Joint Commission for the Accreditation of Healthcare Organizations (JCAHO), focus has again shifted from such quality assurance activities to organizational approaches to continuous quality improvement. It and others have started accrediting managed care organizations and health networks. Finally, large health care purchasers and patients themselves have developed an interest in quality of care. Many of these efforts to define quality have used preventive measures and simple discrete clinical markers to evaluate care. As purchaser and consumer interests develop evaluation and measurement tools, they often focus on nontechnical areas of health care. Thus, the search for quality has expanded beyond physicians and now involves a variety of agendas.

Although physicians have been involved in the development of all of these quality initiatives, many physicians in practice have viewed the results of these activities with some skepticism. Quality is commonly evaluated across a variety of dimensions including structure, process, outcome, and more recently, appropriateness and necessity. Quality activities have traditionally focused on issues of structure and process. A wide variety of studies have been published that demonstrate the positive effect of quality improvement activities on the process of care; however, most of these studies were done at a single facility, limiting their general applicability. Using the other dimensions of quality, such as outcome and issues of appropriateness and necessity, to demonstrate and evaluate the quality of care has proved much more difficult. Physicians, however, place greater value in outcomes-based information. Although Wennberg and others have shown that medical interventions and care for similar conditions can vary dramatically across organizations,[3] the solutions to such problems have proved more elusive. Attempts by national organizations to develop and implement practice guidelines across broad regions have not been uniformly successful. Lomas and colleagues studied the implementation of obstetric guidelines for cesarean sections developed by a national consensus panel in Canada and found that although most obstetricians were aware of the guidelines and agreed with their content, actual practice changed little.[4] For most physicians, quality improvement activities that demonstrably improve the quality of care from the physicians' perspective continue to be questioned.

The study by Goldman and associates in this issue of THE WESTERN JOURNAL OF MEDICINE provides an interesting snapshot of physician leaders' opinions about the origins of substantial quality-of-care improvements within their facilities.[1] The most important finding of this study is that the vast majority of important improvements were not generated by formal quality improvement processes, but resulted from informal discussion and observation. Local formal quality improvement efforts were more likely to result in a clinically important improvement in care and require less staff resources than externally driven formal quality improvement initiatives. Finally, traditional medical staff functions contributed minimally to perceived improvements in clinical quality. How should these findings be interpreted? Is quality improvement dead?

Although quality improvement activities are certainly not dead, this study suggests some strategies that will be necessary for these activities to have a more demonstrable and valued effect on the quality of care. First, the role and responsibilities of systems versus their integrated yet autonomous units need to be clearly defined. Health care delivery systems, be they private managed care organizations or public entities such as the Department of Veterans Affairs, need to develop a policy approach that supports an environment where attempts to improve the quality of care are fostered and valued. Attempts to develop centralized, specific, standardized procedural approaches to quality improvement activities will continue to be more resource-intensive with less demonstrable value than locally generated activities. Health systems should also focus on developing a common language (data definitions) and data collecting methods (information systems) throughout their systems and across systems to allow comparisons across sites to be clinically meaningful. Providing clean, comparable data, and the resources to appropriately evaluate these data at the facility levels are fundamental health system responsibilities.

Health systems also need to develop an understanding about the strengths and limitations of continuous quality improvement activities as agents of change in medical care delivery. There is a difference between the concept of quality improvement and the gains in the process of care versus the questionable gains in the results of care. One issue that differentiates medical care from other industries is the great variety in inputs. In business processes, standardization of inputs brings tremendous improvements in processes, cycle times, and output quality. What is so distinctive in medical care is the concept that the more that therapeutic medical care is needed, the less standardized are the various inputs. Severe medical illness has many areas for possible variation: age, sex, chronicity, comorbidity, and others. Primary and preventive care is provided on standardized clinical material, whereas therapeutic medical interventions are provided on highly varied clinical material (patients). This concept explains the tendency of quality improvement activities to focus on business processes rather than clinical therapeutic processes. Also, integrated delivery networks and managed care organizations are best at primary, preventive, and routine care and remain equally troubled by the delivery of medical intervention. This accounts for the ability to manage primary and preventive services and thereby to set a predictable price for a predictable service.

This important differentiation between the practice of

therapeutic medicine and the delivery of primary and preventive care clarifies the implications of some of the findings in the article by Goldman and colleagues.[1] Systemwide initiatives at quality improvement can be effective only when the input can be standardized. When the inputs of patients, professionals, skill sets, and facilities bring variation, then the quality initiative must be viewed at a level that removes important parts of this variation. In addition, preference variation must be identified and resolved, whereas structural variation must be identified and accommodated. Substantial effort in quality improvement activities could be saved if this view was applied to ensure that systemwide efforts are appropriate in given clinical circumstances.

Assessing and improving the processes and, more important, the outcomes of care will continue to be the responsibilities of specific facilities and professional staffs. The ability to identify an opportunity to improve care or implement a guideline may be a systemwide activity, but the assessment and improvement of clinical problems or the implementation of a clinical guideline will continue to succeed or fail based on the evaluation, planning, participation, and motivation of a facility and its staff. The subtle variations in the process of care delivery from site to site will continue to make locally driven activities, built on a foundation of clean, comparable information, the basis of clinically important quality improvement activities for the foreseeable future. Aggregate process and outcome quality evaluations for groups of patients will continue to provide valuable information about the fitness of systems and the possible overuse and underuse of services. The fundamental unit of quality is delivered at the most basic unit of service, the physician-patient interaction. Facility quality initiatives that use system and facility information to enhance and inform the physician-patient interaction are more likely to demonstrably improve the outcomes of care. The challenge for physicians in the future will be to develop formal methods and harness the quality improvement process to capture those ethereal but important changes in care that currently come about through informal observation and discussion.

BRUCE CHERNOF, MD
Olive View–UCLA Medical Center,
UCLA School of Medicine

RONALD L. KAUFMAN, MD, MBA
Chief of Staff
Los Angeles County–USC Medical Center
Associate Dean
University of Southern California (USC)
School of Medicine
Los Angeles, California

REFERENCES

1. Goldman RL, Barbour GL, Ciesco E. Contribution of locally and externally designed quality management activities to hospitals' efforts to improve patient care. West J Med 1997 Feb; 166:110–117

2. Luce JM, Bindman AB, Lee PR. A brief history of health care quality assessment and improvement in the United States. West J Med 1994 Mar; 160:263–268

3. Wennberg JE, Mulley AG Jr, Hanley D, Timothy RP, Fowler FJ Jr, Roos NP, et al. An assessment of prostatectomy for benign urinary tract obstruction: geographic variations and the evaluation of medical care outcomes. JAMA 1988; 259(20):3027–3030

4. Lomas J, Anderson GM, Domnick-Pierre K, Vayda E, Enkin MW, Hannah WJ. Do practice guidelines guide practice? the effect of a consensus statement on the practice of physicians. N Engl J Med 1989; 321(19):1306–1311

Hospital-Based Quality Management: A Program at the Crossroads

OVER THE PAST ten years, the field of hospital quality management has experienced considerable change. Measurement of the outcomes of care has changed from assessing the structural elements of care to measuring patient-centered outcomes and the health of communities. The assessment of clinical practice has grown from ensuring the adequacy of care to developing scientific methods to rapidly improve the process of care through a series of short-cycle studies. Today quality management departments are not only responsible for ensuring adequate inpatient care in hospital settings, they are also being asked to develop a means to demonstrate "high value" (best quality at a competitive price) for integrated delivery systems encompassing many sites and venues of care.

The task of improving quality while lowering costs has spawned a new set of process-improvement methods aimed at enhancing the value of care. Today the adequacy of care can be measured against explicit review criteria derived from evidence-based practice guidelines.[1,2] The analysis of adverse events now uses new techniques of error analysis and systems improvement developed by other industries. The weeding out of "bad apples" has been supplanted by efforts to reduce unnecessary variability through the analysis and elimination of special causes of variation.[3] Fundamental to these changes has been a new recognition that most quality failures stem from dysfunctional systems and not individual culpability. The measurement of the results of care has broadened beyond the documentation of mortality, morbidity, and cost to encompass the assessment of patient satisfaction, functional state, access to care, and the appropriateness of care. There has also been a shift from a mandate to demonstrate our ability to treat disease to the development of our capabilities to reduce health risk factors and promote healthy behaviors.

The study by Goldman and co-workers reported in this issue does an excellent job of showing some of the important issues for quality management in a large health care system during this period of change.[4] This study examined the effect of quality management activities on hospital efforts to improve care through a well-designed survey of department chiefs in medicine, psychiatry, surgery, and ambulatory care at 47 randomly selected Department of Veterans Affairs (VA) medical centers. The intent of the study was to determine the relative contribution of quality management activities to the hospitals' overall efforts to improve care. The study also examined the relative effects of locally designed quality management activities versus those defined by external organizations. There were two major findings from this study: first, that quality management activities contributed to 31% of the patient improvement activities identified by the department chiefs and to 26% of the activities identified in an analysis of hospital documents; and second, that locally designed quality management activities accounted for 68% of the quality management sources of action, whereas quality management activities mandated by external sources, for example, the